Ubiquitin-dependent regulation of COPII coat size and function.

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Public Summary:
Packaging of proteins from the endoplasmic reticulum into COPII vesicles is essential for secretion. In cells, most COPII vesicles are approximately 60-80 nm in diameter, yet some must increase their size to accommodate 300-400 nm procollagen fibres or chylomicrons. Impaired COPII function results in congenital cranial malformation, connective tissue defects, and abnormal absorption of dietary fats and vitamins, but mechanisms to enlarge COPII vesicles have remained elusive. Here, we identified the ubiquitin ligase CUL3-KLHL12 as a regulator of COPII coat formation, and show that monoubiquitylation by CUL3-KLHL12 is essential for collagen export. We conclude that monoubiquitylation controls the size and function of a vesicle coat.

Scientific Abstract:
Packaging of proteins from the endoplasmic reticulum into COPII vesicles is essential for secretion. In cells, most COPII vesicles are approximately 60-80 nm in diameter, yet some must increase their size to accommodate 300-400 nm procollagen fibres or chylomicrons. Impaired COPII function results in collagen deposition defects, cranio-lenticulo-sutural dysplasia, or chylomicron retention disease, but mechanisms to enlarge COPII coats have remained elusive. Here, we identified the ubiquitin ligase CUL3-KLHL12 as a regulator of COPII coat formation. CUL3-KLHL12 catalyses the monoubiquitylation of the COPII-component SEC31 and drives the assembly of large COPII coats. As a result, ubiquitylation by CUL3-KLHL12 is essential for collagen export, yet less important for the transport of small cargo. We conclude that monoubiquitylation controls the size and function of a vesicle coat.